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COMMONWEALTH OF AUSTRALIA

PATENT SPECIFICATION

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Complete Specification Entitled PROSTHESIS FROM FABRICS COATED WITH COLLAGEN.

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Related Art: 267,052(11,943/61) 41.9; 47.7; 87.4; 40.5.

The following statement is a full description of this invention, including the best method of performing it known to me :

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This invention relates to prostheses adapted to be placed in the human body, and to a process for manufacturing the same. More particularly, the invention is directed to prostheses formed of porous, non-absorbable fabric coated with collagen.

For purposes of clarity, the terms used herein are defined as follows:

"Tendon collagen fibril" means a thread-like collagen structure derived from beef tendon that is round in cross section. These fibrils in the completely dehydrated state generally measure ~~about~~ 500 to 2000 Angstroms in diameter.

"Swollen tendon collagen fibril" means a collagen fibril derived from beef tendon that has been swollen in acid solution. The diameters of swollen collagen fibrils generally range from less than 5000 Angstroms to ~~about~~ 90,000 Angstroms.

"Monofilament" means a single thread of oriented collagen fibrils as extruded through a single orifice in a spinnerette.

"Multifilament" means a group of individual separate collagen monofilaments extruded through a spinnerette. ~~Further details are provided in related application Serial No. 216,247, filed August 10, 1962.~~

"Strand" means a group of collagen monofilaments that have been united to form a unitary structure.

"Tape" means a group of individual collagen monofilaments that have been united to form a unitary structure that is ribbon-like in shape.

"Non-absorbable fibers" means those fibers, synthetic or natural, which are not absorbed in an animal body, particularly a human body, when present therein over an extended period of time. A "non-absorbable fabric" is a fabric formed of non-absorbable fibers.

"Associations of collagen and non-absorbable fibers" means a combination of collagen filaments or strands and one or more non-absorbable fibers, formed, for example, by weaving, knitting, braiding or crocheting, the filaments or strands and fibers together into articles including tubes, which can be straight or Y-shaped.

In the surgical repair of hernias, tantalum gauze and inert fabrics have found considerable use, particularly in older patients who are recognized to have a reduced ability to rebuild tissue at the point of surgery. Tantalum gauze, however, has the undesirable property of becoming brittle and can curl up within the body, causing discomfort. Inert fabric prostheses have the disadvantage that they do not become a part of the

body tissue. During surgery, some surgeons have tried to overcome this disadvantage by knotting catgut sutures randomly throughout the fabric prosthesis. However, this does not result in a uniformly integrated fabric prosthesis. Many inert fabric inserts frequently remain surrounded by a pool of sera after the healing process. A suitable prosthesis for strengthening the repair should be non-toxic, flexible and porous. The ideal prosthesis should retain its strength permanently in intimate contact with body fluids and should be readily accepted and incorporated into the tissues. Porosity is an important characteristic of such a prosthesis to avoid the formation of fluid pockets and to promote the growth through the fabric of repair tissue.

A primary object of the invention, therefore, is to provide a porous, non-absorbable fabric compatible with an animal body, and coated with collagen. A further object is to provide a porous, non-absorbable fabric which is coated with collagen and the pores of which are free of collagen. Another object is the provision of prostheses comprised of the fabric so coated with collagen and promoting the growth of body tissue into and through the prostheses during the healing process.

Still another object is the provision of a process for manufacturing the prostheses of this invention. And

another object is the provision of a process for pretreating the fabric in the manufacture of the prostheses.

Additional objects will be apparent from the following discussion.

The foregoing objects are realized (in accordance with this invention) by providing an improved prostheses comprised of a porous, non-absorbable fabric, stulle or tube coated with collagen, the pores of the fabric being free of collagen. It is an essential feature of the new prostheses that the pores thereof are open and not rendered blood tight by collagen fibrils.

The prostheses of this invention are formed, for example, by knitting, weaving, braiding or crocheting non-absorbable fibers into the shape or form desired. The fibers are not absorbed by an animal body, as the human body, when present therein over extended time intervals, such as a decade. Examples of suitable materials are VINYON-N (Registered Trade Mark), a resin manufactured by the Carbide and Carbon Corporation by copolymerizing vinyl chloride and acrylonitrile; SARAN (Registered Trade Mark), a vinyl chloride polymer manufactured by the Dow Chemical Company; nylon, a polyamide resin made by polymerization of the hexamethylene diamine salt of adipic acid; ORLON (Registered Trade Mark), a synthetic

fiber made from polyacrylonitrile; DACRON (Registered Trade Mark), a synthetic fiber made from terephthalic acid and ethylene glycol; TEFLON (Registered Trade Mark), a tetrafluoroethylene polymer; polyolefins such as polyethylene and polypropylene; cotton and silk. Nylon, ORLON (Registered Trade Mark), DACRON (Registered Trade Mark) and TEFLON (Registered Trade Mark) are products of the E. I. du Pont de Nemours & Co. Preferred herein are DACRON, TEFLON and polyolefins.

It is to be understood that the non-absorbable fibers used herein can be for example, knitted, woven, braided or crocheted into forms suitable for porous implants, in many manner known in the art, since such does not form a part of this invention.

Collagen used herein to coat the non-absorbable fabric corresponds to the type of connective tissue normally laid down by the body during the healing process. Thus, the collagen coating serves as a stimulus for body response during the post-operative period. The porous character of the fabric allows for rapid in-growth of fibroblasts and endothelial cells. All such features combine in concert to make possible rapid and satisfactory attachment of the prosthesis to the host tissues.

Collagen can be prepared as described in United States Patent No. 2,920,000 of H. R. Hochstadt and E. R. Lieberman. Since it is difficult to prepare a collagen dispersion containing more than 2 per cent collagen because of extremely high

viscosities of more concentrated dispersions, the collagen dispersions used in this invention generally contain from 0.1 to 2 per cent by weight of collagen. The vehicle or liquid containing collagen can be one of a wide variety of materials, including: alcohols such as methanol; aqueous solutions of perfluoroacids, as shown in U. S. Patent Nos. 2,919,998 and 2,919,999; and aqueous cyanoacetic acid. Particularly preferred herein are collagen dispersions in a mixture of methanol and aqueous cyanoacetic acid.

The non-absorbable fabric, as in film or mesh form, can be coated with collagen by a number of techniques. The fabric can be immersed in a collagen dispersion for a suitable period of time, and the fabric can then be removed and allowed to drain and dry. Collagen is neutralized after the coated fabric is dry. Alternatively, a dispersion of collagen can be sprayed onto the fabric, followed by draining of the sprayed fabric.

When the fabric is immersed in a collagen dispersion, the fabric is coated with collagen and is thereafter treated to remove collagen present in the pores thereof. This is accomplished advantageously by directing a stream of inert gas against the coated fabric, particularly through the coated fabric. The stream is so adjusted that collagen held in the pores of the coated fabric is removed, while collagen coating the fabric

structure is retained. There is little danger that the collagen coat will be removed from the fabric, since a relatively strong bonding of collagen and the fabric obtains. Representative of inert gases useful herein are air, nitrogen, and carbon dioxide. Since air is inexpensive and advantageous, it is preferred.

Still other techniques can be used herein. A fabric treated with collagen can be dried and then perforated to remove collagen from the pores thereof.

Temperatures of the impregnation step, draining (if such is used), neutralization and removal of collagen from the pores, are generally below ~~about~~ 30°C. in each operation to avoid extensive degradation of collagen. Preferred for each operation are temperatures below ~~about~~ 25°C.

It is to be understood that any of the known tanning agents for use with collagen can be used herein. Chromium, formaldehyde or polyhydroxyphenols ~~etc.~~ can be used alone or in combination. Particularly preferred, however, are the tanning procedures described in U.K. Patent Specification No. 943,170. ~~related applications Serial Numbers 85,289 and 85,302, both filed January 27, 1961.~~

In conjunction with the process for coating a non-absorbable fabric with collagen, it has been discovered that a firmer bonding of collagen and the fabric results when the fabric is pretreated. The pretreatment involves successive

contact with a solvent (A) for hydrophilic materials and a solvent (B) for hydrophobic materials. Solvents (A) and (B) are those which do not dissolve or attack the fiber. Solvents falling within category (A) include water and dilute aqueous solutions containing a detergent, among which are sulfates such as sodium lauryl sulfate, sulfonates such as sodium dodecyl benzene sulfonate, phosphates such as sodium tripolyphosphate, polyoxyalkylene derivatives of a hydroxy compound such as a condensate of 1 mol of nonyl phenol with 9 mols of ethylene oxide and quarternary ammonium compounds such as cetyltrimethylammonium chloride, etc. Representative of solvents (B) are: alcohols, typified by methyl, ethyl, n-propyl, isopropyl, n-butyl, secondary- and tertiary-butyl, etc.; ketones, typified by acetone, methyl ethyl, methyl n-propyl, diethyl, etc.; ethers, typified by dimethyl, diethyl, ethyl methyl, etc. Generally, a large amount of solvent ~~excess of one or more solvents~~ are (A) and ~~of one or more~~ solvents (B) is used in the pretreatment of a non-absorbable ~~adsorbable~~ fiber. Pretreatment is conducted at temperatures from about 40°C. to about 100°C., for time intervals ranging from about 60 minutes to about 1 minute with each solvent, (A) and (B); preferred conditions are the ~~approximate ranges~~ at a temperature of 60-70°C., for 10-5 minutes.

The present invention is more fully described and exemplified in the following examples. It is to be understood,

however, that my invention is not to be limited to any specific form or materials or construction set forth in the examples, but is limited solely by the description in this Specification and the appended claims. Throughout the Specification and the examples which follow, all quantities are expressed in parts by weight unless otherwise indicated.

EXAMPLE I

4.33 grams of DACRON (Registered Trade Mark) mesh (40 denier multifilament DACRON 12.5 inch square) was immersed in a gel prepared by diluting a collagen dispersion comprising 0.8 parts of collagen, 0.4 parts cyanoacetic acid, 49.4 parts water and 49.4 parts of methyl alcohol with an equal volume of methyl alcohol at room temperature (20°C.). The mesh was removed from the dispersion and allowed to drain vertically for about five minutes at room temperature. Compressed air was blown through the mesh to remove any collagenous film remaining across the interstices. If the orifice pressure is about 20 lbs. and the orifice is 4 mm. in diameter, a distance of approximately 3" between the orifice and the mesh is advantageous. Using the same orifice at 35 lbs. pressure, approximately 12" is advantageous between the orifice and the mesh. Shorter distances or higher pressures were found to blow too much collagen from the mesh while longer distances and lower pressures did not completely remove the collagen

dispersion from the interstices. The mesh was allowed to dry for several hours at room temperature. The collagen on the mesh fabric was then neutralized with 100 parts of 10% aqueous ammonia and was tanned with 100 parts formaldehyde (1% aqueous solution). Mesh, so obtained, contains approximately 10% by weight of collagen on the surface of the DACRON (Registered Trade Mark) fibers. When implanted in the subcutaneous tissue of rats, the coated mesh elicited a greater amount of tissue response and fibroplasia than the uncoated mesh and was more readily incorporated by the host tissue.

EXAMPLE II

A piece of DACRON (Registered Trade Mark) mesh (the same size and weight as in Example I) was washed successively with 100 parts of hot water (60°C.), with 100 parts of isopropyl alcohol (25°C.) and 100 parts of acetone (25°C.). It was then dried in the air. The dried mesh was placed in a stainless-steel, TEFLON (Registered Trade Mark) coated tray measuring 15" x 9" x 1/2" containing a 1/8" layer of collagen dispersion containing 0.8 parts of collagen fibrils and 49.4 parts of methyl alcohol, and 49.4 parts of water and 0.4 parts of cyanoacetic acid, and another 1/8" layer of the same dispersion was placed on top of the fabric. The collagen dispersions and mesh were in contact for 24 hours at 25°C. The resulting laminate then was neutralized with 100 parts of 10 per cent aqueous ammonia. It was tanned with 100 parts

of formaldehyde (1 per cent) and removed from the tray. Edges of the mesh were trimmed to remove excess collagen. The laminate was strong, uniform and very resistant to separation. These characteristics continued when the film was wet with water. Only very severe stretching or deformation freed an edge of the collagen from the DACRON (Registered Trade Mark) mesh and, once freed, it resisted further delamination.

It is found that DACRON (Registered Trade Mark) and collagen are more firmly bound by virtue of the pretreatment of DACRON (Registered Trade Mark) than when the pretreatment is omitted. In fact, pretreated DACRON (Registered Trade Mark) and collagen are more firmly bound than when brought together by any other technique.

While the invention has been described in detail according to the articles and manufacture thereof, it is to be understood that changes and modifications can be made (without departing from the spirit or scope of the invention) and it is intended in the appended claims to cover such changes and modifications.

AMENDED

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The Claims defining the invention are as follows :

1. A surgical prosthesis comprising a porous, non-absorbable fabric, tulle or tube coated with collagen, the pores of the fabric being free of collagen. (14-12-1962)

2. The article of Claim 1 wherein the fabric is ~~DACRON as herein defined~~ polyethylene terephthalate. (14-12-1962)

3. The process for manufacturing the surgical prostheses of Claims 1 or 2 which comprises the steps of impregnating a porous, non-absorbable fabric with a dispersion of swollen collagen fibrils and removing collagen from the pores of said fabric while retaining collagen impregnated upon said fabric. (14-12-1962)

4. The process of Claim 3 wherein the removal of the collagen from the pores is effected by blowing the impregnated fabric with a stream of inert gas at a rate sufficient to remove collagen from the pores thereof and insufficient to remove collagen from the fabric. (14-12-1962)

5. The process of Claim 4 wherein the inert gas is air. (14-12-1962)

6. The process of Claim 3 wherein the fabric is pretreated successively with a solvent (A) for hydrophilic materials and a solvent (B) for hydrophobic materials. (14-12-1962)

7. The process of Claim 6 wherein treatments with solvent (A) and with solvent (B) are made at temperatures between about 40°C. and about 100°C. for time intervals ranging from ~~about 60 minutes to about 2 minutes~~. (14-12-1962)

8. The process defined in Claim 6 wherein solvent (A) is water. (14th December, 1962)

9. The process defined in Claim 6 wherein solvent (B) is isopropyl alcohol. (14th December, 1962)

10. A surgical prosthesis substantially as described herein in any one of the Examples. (14th December, 1962)

11. A process of making a surgical prosthesis substantially as described herein in any one of the Examples. (14th December, 1962)

Dated this 19th day of December, 1963.

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By their Patent Attorneys:

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